

## **REMARKS/ARGUMENTS**

In response to the Notice of Non-Compliant Amendment mailed March 3, 2004, Applicant respectfully affirms the provisional election to prosecute the invention of Group I made during a telephonic interview with the Examiner on March 14, 2003. Claims 45, 54, 55, 59, and 60 have been canceled. Claims 37-44, 111-125, and 127-130 remain in this application. Claim 42 has been amended in order to place the claim in proper dependent form in compliance with 37 CFR 1.75(c) and to further clarify Applicant's inventive concept. Claims 43, 44, 111-125, and 127 have herein been amended to point out and clarify that the instantly disclosed and claimed chondroitin polymer is unsulfated.

Submitted February 6, 2004 was is a Supplemental Information Disclosure Statement in which the prior art contained herein are relevant. A prior art search was conducted within the last thirty days and, hence, such prior art is timely submitted. Applicant respectfully requests that the Examiner consider each article submitted herein and pass claims submitted herein to issuance in view thereof.

### **Election Requirement**

Applicant respectfully affirms the provisional election without traverse to prosecute the invention of Group I (claims 37-45, 54, 55, 59, 60, 111-125, and 127-130) made during a telephonic interview with the Examiner on March 14,

2003. In view of the cancellation of claims 45, 54, 55, 59 and 60 made herein, Applicant respectfully requests such election be entered and claims 37-44, 111-125, and 127-130 be passed to issuance in view of the remarks made herein.

Objection under 37 CFR 1.75(c)

In the Office Action mailed September 9, 2003, claim 42 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of the previous claim. Applicant respectfully submits that claim 42 has been amended to place the claim in proper dependent form. In view of the amendment to claim 42 made herein, Applicant respectfully requests withdrawal of the objection to claims 42, 54, 55, 59 and 60.

First Rejection under 35 U.S.C. § 102(b)

In the Office Action mailed September 9, 2003, claims 37-41, 43, 44, 45, 111-125, and 127-130 were rejected under 35 U.S.C. § 102(b) as being anticipated by Sugumaran et al.

Contrary to the Examiner's assertions, the Sugumaran et al. reference does not describe, identify, or even suggest a recombinantly produced, unsulfated chondroitin polymer and the enzyme (and methodology) that makes the unsulfated chondroitin polymer chains (i.e. chondroitin synthase). Prior to

Applicant's priority date, all known forms of the chondroitin polymer were chemically modified; either sulfated— a chondroitin proscribed by the production of the chondroitin polymer in its natural host (i.e. vertebrate, bacterial) or fructosylated in its natural host (i.e. *E. coli* K4 bacteria). Never before had an unsulfated chondroitin polymer been isolated and purified from a recombinant process. The Sugumaran et al. reference merely describes some properties of a semi-purified, unknown enzyme (e.g., no DNA or protein sequences disclosed) that adds on only a single sugar, GlcUA, to existing, sulfated chondroitin-like polymer chains. The enzyme disclosed in Sugumaran et al. is "GlcA transferase II", not a chondroitin synthase which is a dual-action GlcA and GlcNAc transferase and the polymer described is a sulfated polymer. This identification was based on defined biochemical assays in vitro with various substrates and precursors used by many skilled in the art. The GlcA transferase II disclosed in Sugumaran et al. is only one potential part of the vertebrate chondroitin biosynthesis pathway and would not be capable of producing an unsulfated chondroitin polymer by repetitive sugar addition.

Prior to Applicant's priority filing date of April 25, 2000, and the publication of "Identification and molecular cloning of a chondroitin synthase from *Pasteurella multocida* type F", DeAngelis and McCue, J. Biol. Chem. 275(31):24124-241 (August 2000), no other chondroitin synthase had ever been definitively identified by amino acid sequence, gene sequence, and/or

functional expression studies in a foreign host. Consequently, no recombinantly produced unsulfated chondroitin polymer could ever have been produced and the Sugumaran et al. reference is no different.

Consequently, the Sugumaran et al. reference does not put one of ordinary skill in the art in the possession of a recombinantly produced, unsulfated chondroitin polymer and particularly does not disclose Applicant's purified composition.

In view of the above, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 37-41, 43, 44, 45, 111-125, and 127-130 under 35 U.S.C. § 102(b) and respectfully requests such claims be passed to issuance.

#### Second Rejection under 35 U.S.C. § 102(b)

In the Office Action mailed September 9, 2003, claims 42, 54 and 59 were rejected under 35 U.S.C. § 102(b) as being anticipated by Casu et al. (US 5,008,253).

For the reasons set forth below, the rejection of claims 42, 54 and 59 is respectfully traversed. Applicant respectfully submits that the Casu et al. reference merely describes the sulfation of various sugar polymers by chemical means known to many skilled in the art including reagents such as chlorosulfonic acid and sulfuric anhydride (trioxide) complexes. However, the

chondroitin-based starting materials used by Casu et al. were not unsulfated chondroitin. Once again, prior to Applicant's priority date (the first time anyone identified definitively, by chemical and enzymatic analyses, the *Pasteurella multocida* Type F as a source of unsulfated chondroitin polymers) a naturally occurring, completely unsulfated chondroitin polymer was not known or disclosed in the prior art. Harsh chemical desulfation procedures may be used to remove a large fraction of sulfates, but complete desulfation results in polymer chain breaks (depolymerization). The chondroitin-based materials in the Casu et al. reference are found in a natural state of sulfation and subsequently chemically oversulfated.

In view of the above, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 42, 54 and 59 under 35 U.S.C. § 102(b) and respectfully requests such claims be passed to issuance.

#### Third Rejection under 35 U.S.C. § 102(b)

In the Office Action mailed September 9, 2003, claims 42, 55 and 60 were rejected under 35 U.S.C. § 102(b) as being anticipated by Skjak-Braek et al. (US 4,990,601).

For the reasons set forth below, the rejection of claims 42, 55 and 60 under 35 U.S.C. § 102(b) is respectfully traversed. Contrary to the Examiner's assertions, the Skjak-Braek et al. reference teaches a sulfated chondroitin

polymer (chondroitin sulfate) rather than unsulfated chondroitin polymer as disclosed in Applicant's invention. Further, the Skjak-Braek reference only teaches the partial epimerization of a polymer with mannuronic acid, not uronic acids in general and only draws inference to the fact that the process may work using glucuronic acid. In the field, it is known that the sugar's relative stereochemistry (i.e. mannose versus glucose based monomers) often drastically changes their properties and/or reactivity. This observation is one reason carbohydrate chemistry is often very difficult. Thus, the method has not been rigorously proven for chondroitin (contains glucuronic acid).

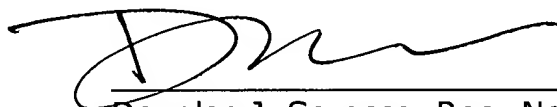
In view of the above, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 42, 55 and 60 under 35 U.S.C. § 102(b) and respectfully requests such claims be passed to issuance.

### Conclusion

It is respectfully submitted that this application, as now amended, is in condition for allowance for the reasons stated above. Therefore, it is requested that the Examiner reconsider each and every rejection as applicable to the claims now pending in the application and pass such claims to issue.

This amendment is intended to be a complete response to the Notice of Non-Compliant Amendment dated March 3, 2004. In the event that any outstanding issues remain that would delay the allowance of this application, the examiner is urged to contact the undersigned to telephonically discuss such outstanding issues.

Respectfully submitted,



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